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EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	8

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/866,801	Applicant(s) CHERWONOGRODZKY, JOHN W.	
	Examiner Vanessa L. Ford	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This Office Action is responsive to Applicant's response filed April 29, 2002. Claims 13-29 have been cancelled. Claims 30-46 have been amended. An action on the merits of claims 30-46 is contained herein below.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

OBJECTIONS/REJECTIONS WITHDRAWN

3. In view of Applicant's amendment the following Objections and Rejections have been withdrawn:

a) Objection of claims 26 and 27, page 3, paragraph 2 of previous Office action.
b) Rejection of claim 28 under 35 U.S.C. 101, page 3, paragraph 3 of the previous Office action.
c) Rejection of claim 18 under 35 U.S.C. 112, second paragraph, page 7, paragraph 5 of the previous Office action.
d) Rejection of claim 24 under 35 U.S.C. 112, second paragraph, page 7, paragraph 6 of the previous Office action.
e) Rejection of claim 25 under 35 U.S.C. 112, second paragraph, page 8, paragraph 7 of the previous Office action.
f) Rejection of claim 26 under 35 U.S.C. 112, second paragraph, page 8, paragraph 8 of the previous Office action.
g) Rejection of claims 13-18, 27 and 29 under U.S.C. 102(b), pages 12-13, paragraph 11 of the previous Office action.

REJECTIONS MAINTAINED

4. The rejection under 35 U.S.C. 112, first paragraph is maintained for newly presented claim 45 for the reason set forth on pages 2-7 of the previous Office Action.

The rejection was on the grounds that the specification, while being enabling for fungal and yeast cell culture supernatants, does not reasonably provide enablement for a vaccine comprising the fungal and yeast cell culture supernatants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claim 45 is drawn to a vaccine comprising fungal or yeast cell culture supernatants.

The specification fails to teach how to formulate the claimed vaccines. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to a fungal or yeast infection or disease induction. The specification teaches that the claimed fungal or yeast supernatants containing antigenic components were used to vaccinate mice over a 10 week period. The specification merely states" that there was "considerable variation" of the response of mice to the different vaccinations cited in Table VI" (page 17).

The specification does not disclose how to formulate the fungal or yeast vaccine nor does the specification teach what dosages are required to treat a patient with a fungus or yeast infection? The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of treating fungal or yeast infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced. The specification further does not disclose what mode of administration can be used in regard to the vaccines to be capable of reaching the target organs necessary to treat a particular fungal or yeast infection. Therefore, it is unclear as to how to formulate a vaccine which will treat <u>any</u> fungal or yeast infection.

The ability to reasonably predict the capacity of a single bacterial immunogen or combinations of immunogens to induce protective immunity from *in vitro* antibody reactivity studies is problematic. Otcenasek et al *(Vet Med (Praha) April 1981 26(4): 193-202)* suggests that are theoretical problems of the nature and duration of immunity in regard to fungal vaccines (see the Abstract). Deepe, Jr., *(Clinical Microbiology Reviews, Oct. 1997, p.585-596)* teaches that historically vaccines used for coccidioidomycosis have failed. Deepe, Jr. teaches that fungal vaccines that can be formulated for human use are problematic. Deepe, Jr. teaches that concept of fungal

vaccination for humans remains viable but has not attracted much attention because of the relatively low incidence of infection and the geographic distribution of several fungi compared to many viral and bacterial diseases (page 586). Deepe, Jr. teaches that one of the major problems exists with the formulation of fungal vaccines is that there are no motifs or canonical sequences exist that distinguish a protective fungal antigen from one that is not. Deepe, Jr. teaches that the concepts of how to determine if a gene or its product can mediate protection must be take into consideration the method in which the immunogen is administered *in vivo*. Deepe, Jr., teaches that another potential problem exists in regard to using recombinant technology in establishing fungal vaccines. Deepe, Jr. teaches that production of peptides or small protein fragments may not be able to be expressed by prokaryotic expression systems because of size. Deepe , Jr. further teaches that fungal vaccination of immunocompromised host are problematic because most vaccines that elicit protective antibodies strictly rely on cellular immunity. Deepe, Jr. teaches vaccines that rely on cellular immunity may be none effective in an immunocompromised host (see page 593).

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a fungal or yeast vaccine that would achieve a desire level of success when administered to a patient with a fungal or yeast infection that is capable of treating that fungal or yeast infection, 3) there are limited working examples which suggest the desired results of a successful vaccine that is to treat any fungal or yeast infection, 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that it would require undue experimentation to make and use the claimed invention.

Applicant urges that the rejection of claim 28 in the previous Office action (Paper No. 7) is moot. Claim 28 has been cancelled.

Applicant's arguments filed April 29, 2002 have been fully considered but is not persuasive. The Examiner agrees that the rejection under 112, first paragraph for claim

28 is moot. However, newly presented claim 45 is drawn to a vaccine comprising a fungal or yeast cell culture supernatant. It is the Examiner's position that there is nothing on the record to show that the specification is enabled for a vaccine comprising a fungal or yeast cell culture supernatant because the specification fails to provide substantive evidence that the claimed vaccines are capable of inducing protective immunity.

5. The rejection under 35 U.S.C. 102(b) of newly presented claims 30-36, 40-41 and 45-46 as anticipated by Pasarell et al is maintained for the reason set forth on pages 2-7 of the previous Office Action.

The rejection was on the grounds that Pasarell et al teach concentrated culture filtrate antigens that were obtained from the genera *Alternaria, Bipolaris, Curvularia, Dactylaria, Drechslera, Embellisia, Exserohilum, Fusarium, Helminthosporium, Microsporum, Scolecobasidium and Scopulariopsis*. Pasarell et al teach that the culture antigens were incubated and aerated on a rotating shaker (p. 1655, 2nd column). Pasarell et al teach that the concentrated culture filtrate antigens was used to immunize two New Zealand White female rabbits. Pasarell et al teach that an emulsion of 1 ml of each control antigen and 1 ml of Freund incomplete adjuvant was injected intramuscularly into the New Zealand rabbits. *Alternaria, Dactylaria, Drechslera, Embellisia, Fusarium, Micosporum, Scolecobasisum and Scolecobasidium and Scopulariopsis* did not have common antigens when tested against the antisera. Antigens of *Helminthosporium* only reacted with its own sera and there were no cross-reactions with any other antigens tested (p. 1656, 1st column). Pasarell et al teach that antisera prepared from *E. rostratum* recognized antigens prepared from *E. holmii*. Pasarell et al teach that a similar result was observed with antisera prepare from *E. mcginnisii* and *E. longirostratum*. Pasarell et al that common antigens are shared between the genera of *Bipolaris* and *Curvularia* (p. 1656). The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not

changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). The fungal or yeast culture of Pasarell, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that the rejection of claims 13-20, 22-24, 26 and 28-29 in the previous Office action (Paper No. 7) is moot. Claims 13-20, 22-24, 26 and 28-29 have been cancelled. Applicant urges that the term "generic" in Pasarell et al was use to describe "genus" specific antigens whereas the term in the instant invention the term "generic" in the instant invention means detection of serum antibodies to a large panel of different species. Applicant urges that *Bipolaris* and *Curvularia* cross-reacted but once belonged to a single genus. Applicant urges that *Yersinia enterocolitica* and *Pasteurella pestis* were members of separate genuses until it was found that they belong to the same genus, *Yersinia*. Applicant urges that Paserell et al teach that concentrated filtrate antigens that were filtered using an Amicon with PM 10 filter would cause loss of toxins and antigen of less than 10,000 molecular weight. Applicant urges that the instant invention provides a far more superior method which uses undiluted, unconcentrated filtrate and provides greater applications. Applicant urges that the Pasarell et al assay was used to assess rabbits injected with 20-fold concentrated antigen given with adjuvant oils intramuscularly and intravenously. Applicant urges that

the claimed invention was used to assess patient sera where 30% were found to have antibodies to *Chaetomium*. Applicant urges that Pasarell discussed some positive reactions but there are a lot of zero reactions. Applicant urges that the method of detecting between Pasarell et al and the Applicants invention are very different. Applicant urges that Pasarell et al used agar immunodiffusion and that this method is impractical in a diagnostic laboratory for assessing several sera whereas ELISA detection is less subjective, more sensitive and capable of assessing more serum samples.

Applicant's arguments filed April 29, 2002 have been fully considered but they are not persuasive. The Examiner agrees that the rejection under 35 U.S.C. 102 (b) of claims 13-20, 22-24, 26 and 28-29 is moot, since claims 13-20, 22-24, 26 and 28-29 have been cancelled. However, newly presented claims 30-36, 40-41 and 45-46 are drawn to a fungal or yeast cell culture supernatant. It is the Examiner's position that there is nothing on the record to show that the fungal cell culture supernatants of the prior art are not the same as the claimed invention. The claims are drawn to a fungal or yeast cell culture supernatant. Applicant appears to be arguing limitations that are not in the claims such as the molecular weight of the antigens, the use of the antigens (i.e to detect rabbit verses human sera) or the method of used to detect the antigens (immunodiffusion verses ELISA). Therefore, the teachings of the prior art anticipate the claimed invention.

6. The rejection under 35 U.S.C. 102(b) as anticipated by Calera et al is maintained for newly presented claims 30-35, 41 and 46 for the reason set forth on pages 11-12, paragraph 10 of the previous Office Action.

The rejection was on the grounds that Calera et al teach cell culture supernatants obtained from *Aspergillus* (see the Abstract and page 2324). Calera teach that *Aspergillus nidulans* antigens elicit antibodies in rabbits. Calera et al teach that the *Aspergillus nidulans* antigens cross-reacted with antigens from *A. fumigatus, A. flavus, A. terreus, A. clavatus* and *A. niger* (p. 2331). Calera et al teach that screening a battery of 10 selected human serum samples from patients with aspergilloma or invasive aspergillosis demonstrated that two antigens from stationary-phase culture supernatants were consistently reactive (see the Abstract). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins are obtained from microorganisms of the genera *Aspergillus*. The process limitation of the supernatant being prepared and used at 20°C is a matter of design choice. Although the reference appears to disclose the same cell culture supernatant claimed by the Applicants, the reference does not disclose the cell culture supernatant being prepared at the same temperature as the claimed process. However, the production of a cell culture supernatant by a particular process does not impart novelty or unobviousness to a cell culture supernatant when the same cell culture supernatant is taught in the prior art. This particularly true when properties of the cell culture supernatant are not changed by the process in an unexpected manner. See In re Thorpe, 227 USPQ 964 (CAFC 1985); In re Marosi, 218 USPQ 289, 292-293 (CAFC 1983); In re Brown, 173 USPQ 685 (CCPA 1972). It would be inherent that the reference of the prior art would detect aflatoxins. The fungal or yeast culture of Calera, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that there are many notable difference and limitations of the work done by Calera et al and the claimed invention. Applicant urges that Calera et al dealt only with proteins and Applicant found that in protein digestion that only about 10-20%

of the antigen was protein. Calera et al disclosed a method using crude fungal supernatants which were freeze-dried and Applicant notes that the antigens are inactivated by freezing and the aflatoxins would be lost by being dialyzed and that acetone would remove the fats and the hydrophobic ring of aflatoxins. Applicant urges that Calera et al disclosed antigens expressed on or in the fungal cell and the Applicants teach that mice were immunized with whole killed cells and their sera was tested on ELISA plates coated with culture supernatants. Applicant urges that the screening of human serum samples from patients with aspergilloma was actually inconsistent.

Applicant's arguments filed April 29, 2002 have been fully considered but they are not persuasive. The Examiner agrees that the rejection under 35 U.S.C. 102 (b) of claims 13-22, 24-25 and 29 is moot, since claims 13-22, 24-25 and 29 have been cancelled. However, newly presented claims 30-35, 41 and 46 are drawn to a fungal or yeast cell culture supernatant. It is the Examiner's position that there is nothing on the record to show that the fungal cell culture supernatants of the prior art are not the same as those set forth in the claimed invention. The instant claims are drawn to a fungal or yeast cell culture supernatant. Applicant appears to be arguing limitations that are not in the claims such as the molecular weight of the antigens and the use of the antigens. It should be remember that the claims are drawn to a product and "the use of the fungal cell culture supernatant as an antigenic soured for detecting the level of antibodies from a sample test subject" is an intended use limitation. Limitations such as "the supernatant is prepared and used at a temperature above freezing", "the supernatant is

prepared and used at 20°C", "the supernatant is prepared under aeration condition" and the "supernatant is prepared by gentle shaking" are viewed as design choice limitations. Since intented use and non-critical reaction conditions are afforded no patentable weight, the teachings of Calera et al do anticipate the instantly claimed invention.

NEW GROUNDS OF REJECTION NECESSIATED BY AMENDMENT

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

7. Claims 30-35, 37-39, 41 and 45-46 are rejected under 35 U.S.C. 102(e) as anticipated by Takesako et al, *(U.S. Patent No. 6,333, 164, published December 25, 2001).*

Claims 30-35, 37-39, 41 and 45-46 are drawn to a fungal or yeast cell culture supernatant as antigenic sources for detecting levels of antibodies from a sample test subject.

Takesako et al teach the preparation of fungal antigens (i.e. *Candida albicans, Cryptococcus neoformans and Aspergillus fumigatus*). Takesako et al teach that the fungal antigens where suspended in Potato-Dextrose medium and subject to shaking overnight (column 27, lines 3-6). Takesako et al teach that *Candida* serum exhibited cross reactivity to proteins derived from *Cryptococcus neoformans* and *Aspergillus* (column 38, lines 25-28). Takesako et al teach that *Aspergillus* serum showed crossreactivity with *Cryptococcus* (column 38, lines 39-41). Takeaako et al teach fungal antigen solutions that are mixed with equal volumes of incomplete Freund's adjuvant yield a water-in-oil vaccine preparation (column 28, lines 59-62). Limitations such as "the supernatant is prepared and used at 20°C" are viewed as a matter of design choice.

Since the Office does not have the facilities for examining and comparing applicant's fungal or yeast culture supernatant with the fungal or yeast culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal or yeast culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal or yeast culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 30-41 and 45-46 are rejected under 35 U.S.C. 102(b) as anticipated by Manning et al *(The Laryngoscope, 108, October 1998)*.

Claims 30- 41 and 45-46 are drawn to a fungal or yeast cell culture supernatant as antigenic sources for detecting levels of antibodies from a sample test subject.

Manning et al teach the use of Bipolaris, *Helminthosporium, Curvularia, Alternaria and Aspergillus* cultures in skin tesing. Manning et al teach the antigens were injected in the upper back of patients with n test applicator (1489, 2nd column). Manning et al teach described modified RAST testing to fungal antigen in a consecutive series of allergic fungal sinusitis (AFS) patients. Manning et al teach that patients culturing a dematiaceous mold usually *(Bipolaris*) all reacted to at least one dematiaceous mold in the RAST panel, which included *Helminthosporium* antigen, *C. lunata* and *Alternaria tenuis*. Manning et al teach that the patients reacted most strongly to the *Helminthosporium* antigen indicate a probable high degree of crossreactivity between *Helminthosporium* and *Bipolaris* (page 1488, 1st column). Manning et al teach that patients that have positive skin test reactions to *Bipolaris* antigen all demonstrated Bipolaris-specific IgE and IgG antibodies(1494, lst column). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins are obtained from microorganisms of the genera *Aspergillus*. Limitations such as "the supernatant is prepared and used at a temperature above freezing", "the supernatant is prepared and used at 20°C", "the supernatant is prepared under aeration condition" and the "supernatant is prepared by gentle shaking" are viewed as limitation of design choice. The limitation of "detecting level of antibodies from a sample test subject" is a limitation of intended use.

Since the Office does not have the facilities for examining and comparing applicant's fungal culture supernatant with the fungal culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

9. Claims 30-34, 41, 44 and 46 are rejected under 35 U.S.C. 102(b) as anticipated by Malling et al *(Allergy, 1986, 41, 57-67).*

Claims 30-34, 41, 44 and 46 are drawn to a fungal or yeast cell culture supernatant as antigenic sources for detecting levels of antibodies from a sample test subject.

Malling et al teach the use of a *Cladosporium herbarum* antigen (see the Abstract and page 58). Malling et al teach that using bronchial provocation test (BPT) a positive (test for antigen) was found in three patients clinically classified as inconclusive 3/ 11 patients tested) or 27% "false positive". Malling et al teach that the skin prick test (SPT) results showed positive tests in two patients (2/11 patients tested) or 18% "false positive". Malling et al teach that the histamine release from basophil granulocyes (HIST) test results showed positive tests in two patients (2/11 patients test) or 18% "false positive" (see the Abstract and pages 61-62). Limitations such as "the supernatant is prepared and used at a temperature above freezing", "the supernatant is

prepared and used at 20°C", "the supernatant is prepared under aeration condition" and the "supernatant is prepared by gentle shaking" are viewed as limitations of design choice. The limitation of detecting level of antibodies from a sample test subject" is a limitation of intended use.

Since the Office does not have the facilities for examining and comparing applicant's fungal culture supernatant with the fungal culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e.,that the fungal culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

10. Claims 30-36, 41-42 and 45-46 are rejected under 35 U.S.C. 102(b) as anticipated by van der Heide et al *(Allergy, 1985, 40, 592-598).*

Claims 30-36, 41-42 and 45-46 are drawn to a fungal or yeast cell culture supernatant as antigenic sources for detecting levels of antibodies from a sample test subject.

van der Heide et al teach *Aspergillus fumigatus*, *Penicllium notatum*, *Alternaria alternata* and *Cladosporium herbarum* antigenic extracts (see the Abstract and page 593, 1st column). van der Heide et al teach that 3 rabbits were immunized (1 rabbit per fungus) with an antigen mixture in Freund's adjuvant (page 593). It would be inherent that the *Aspergillus* antigens would be effective in detecting aflatoxins since aflatoxins

are obtained from microorganisms of the genera *Aspergillus*. Limitations such as "the supernatant is prepared and used at a temperature above freezing"and the supernatant is prepared and used at 20°C"are viewed as limitation of design choice. The limitation of detecting level of antibodies from a sample test subject" is a limitation of intended use.

Since the Office does not have the facilities for examining and comparing applicant's fungal culture supernatant with the fungal culture supernatant of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (i.e., that the fungal culture supernatant of the prior art does not possess the same material structural and functional characteristics of the claimed fungal culture supernatant). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
July 12, 2002

JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600